



Q/ Do venlafaxine and gabapentin control hot flashes in women with a history of breast cancer?

EVIDENCE-BASED ANSWER

A | **YES.** Venlafaxine reduces hot flashes more than placebo in women with a history of breast cancer; adverse effects include dry mouth and constipation (strength of recommendation [SOR]: **B**, randomized clinical trials [RCTs] with heterogeneous outcomes).

Gabapentin also reduces hot flashes

more than placebo (SOR: **B**, a single RCT); adverse effects include dizziness and somnolence (SOR: **C**, standard reference). After having tried both medications, women tend to prefer venlafaxine (SOR: **C**, open-label crossover trial).

Treating hot flashes is an off-label use for both drugs.

Evidence summary

A double-blind RCT of 191 women who had been treated for breast cancer (two-thirds were taking tamoxifen) and were having at least 14 hot flashes per week randomized the women to one of 4 groups: once-daily extended-release venlafaxine at 37.5, 75, or 150 mg, or placebo.¹ Higher doses of venlafaxine produced greater reductions in hot flash scores from baseline than did the lowest dose or placebo: 150 mg lowered scores by 61% (95% confidence interval [CI], 48%-75%); 75 mg also decreased scores by 61% (95% CI, 50%-68%); 37.5 mg reduced scores by 37% (95% CI, 26%-54%); and placebo lowered scores by 27% (95% CI, 11%-34%).

At the 75- and 150-mg doses, the number needed to treat to reduce the number of hot flashes by 50% was about 3. However, these doses caused dose-dependent adverse effects, including dry mouth, constipation, nausea, and decreased appetite, whereas the lowest dose produced an adverse-effect rate equal to placebo (no statistics supplied for these comparisons).

Venlafaxine significantly decreased the frequency of hot flashes

A pair of double-blind RCTs, reported together, evaluated hot flash frequency among 77 breast cancer survivors with at least 7 hot flashes a week who took either extended-release venlafaxine (37.5 or 75 mg daily) or placebo for 6 weeks.² Patients then crossed over to take either venlafaxine or placebo for another 6 weeks. Compared with placebo, venlafaxine 37.5 mg reduced the mean daily hot flash frequency by 22% ($P<.001$); venlafaxine 75 mg reduced it by 14% ($P<.013$).

In an open-label case series, 40 breast cancer patients with at least 20 hot flashes per week received extended-release venlafaxine 37.5 mg once daily for 8 weeks.³ Patients reported a 53% reduction in hot flash frequency compared with baseline ($P<.001$).

Gabapentin reduces hot flashes at 300 mg tid

A double-blind RCT of 420 women with breast cancer who had at least 14 hot flashes a week compared the effectiveness of gaba-

Angela Sarkissian, MD;
Jon O. Neher, MD
Valley Family Medicine
Residency, Renton, Wash

Ravipal Singh, PharmD
University of Washington
Medicine/Valley Medical
Center, Renton, Wash

Leilani St. Anna, MLIS, AHIP
University of Washington
Health Sciences
Libraries, Seattle

ASSISTANT EDITOR
Gary Kelsberg, MD
Valley Family Medicine
Residency, Renton, Wash

CONTINUED ON PAGE 772

CONTINUED FROM PAGE 759

pentin 100 mg tid, 300 mg tid, or placebo for 8 weeks.⁴ Investigators found no significant difference between the 100 mg tid dosing and placebo. However, gabapentin at 300 mg tid reduced hot flashes by 44% (an average of 2 fewer per day) compared with placebo ($P<.007$).

The study didn't assess adverse effects, but noted that the withdrawal rates were similar between the groups receiving gabapentin and placebo (12%-17%). An authoritative online reference lists the 2 most common adverse effects of gabapentin as dizziness (11%-28%) and somnolence (5.5%-25%).⁵

Women prefer venlafaxine to gabapentin

A multicenter, open-label crossover trial in-

volving 66 women with a history of breast cancer who had at least 14 hot flashes per week evaluated patient preference when treated with extended-release venlafaxine 75 mg daily and gabapentin 300 mg tid, each for 1 month.⁶ More patients preferred taking venlafaxine than gabapentin (68% vs 32%; $P<.01$), although both treatments reduced the numbers of hot flashes.

Recommendations

In a patient education statement, the American Cancer Society states that women with premature menopause caused by cancer treatment may do well with exercise and relaxation techniques alone. The statement mentions venlafaxine, fluoxetine, and paroxetine as adjunct therapy.⁷

JFP

References

1. Loprinzi CL, Kugler JW, Sloan JA, et al. Venlafaxine in management of hot flashes in survivors of breast cancer: a randomised controlled trial. *Lancet*. 2000;356:2059-2063.
2. Carpenter JS, Storniolo AM, Johns S, et al. Randomized double-blind placebo-controlled crossover trial of venlafaxine for hot flashes after breast cancer. *Oncologist*. 2007;12:124-135.
3. Biglia N, Torta R, Roagna R, et al. Evaluation of low-dose venlafaxine for the therapy of hot flashes in breast cancer survivors. *Maturitas*. 2005;52:78-85.
4. Pandya KJ, Morrow GR, Roscoe JA, et al. Gabapentin for hot flashes in 420 women with breast cancer: a randomized placebo-controlled trial. *Lancet*. 2005;366:818-824.
5. Data for gabapentin side effects from MicroMedX. Available at: <http://www.thomsonhc.com/micromedex2/librarian>. Accessed May 16, 2013.
6. Bordeleau L, Pritchard KI, Loprinzi CL, et al. Multicenter, randomized, cross-over clinical trial of venlafaxine vs. gabapentin for the management of hot flashes in breast cancer survivors. *J Clin Oncol*. 2010;28:5147-5152.
7. American Cancer Society. Sexuality for the woman with cancer: premature menopause. Available at: www.cancer.org/Treatment/TreatmentsandSideEffects/PhysicalSideEffects/SexualSideEffectsinWomen/SexualityfortheWoman/sexuality-for-women-with-cancer-early-menopause. Accessed April 24, 2012.

Managing Hypoglycemia in Primary Care

This supplement on hypoglycemia will help you to:

- ▶ Educate patients about their risk of hypoglycemia
- ▶ Identify risk factors and behaviors that increase the risk of hypoglycemia in patients
- ▶ Compare glucose-lowering agents and the risk of hypoglycemia associated with them



Click on Supplements at jfponline.com or visit <http://www.jfponline.com/Pages.asp?id=10761>

